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Remarks

Claims 1-22 are pending. Claims 1, 6, 12, 15 and 20 have been amended. Claims 1, 6, 12, 15 and 20 were amended to more clearly claim what Applicants consider to be their invention without narrowing any elements or limitations. Claims 7, 13, 14, 17, 19, 21, and 22 were withdrawn by the examiner. Claims 6, 12, 15 and 20 were objected to for including non-elected subject matter.

Election

The examiner acknowledges the election filed 06/12/03 (paper no. 13) by Applicants where Applicants elected with traverse invention II claims 6, 12, 15, 16, 18, and 20 drawn to a peptide of SEQ ID NO: 6 or a fragment thereof.

The examiner states that these claims and linking claims 1-5 and 8-11 are under examination.

Sequence Listing

Applicants note that the examiner states that the previously submitted CRF and Sequence Listing have been entered.

Information Disclosure Statements

Applicants note that the examiner has acknowledged receipt of and consideration of the documents referred to in their IDSs. However, reference B9 on the PTO-1449 (paper no. 9) has not been initialed nor marked through. Applicants assume this was an oversight and that the reference was indeed received and considered. Applicants respectfully request that the examiner initial this reference to indicate receipt and consideration.

Sequence Rule Non-compliance

The examiner states that the specification at line 20 on page 36 and line 31 on page 37 appear to recite an amino acid sequence that is longer than 4 residues in length, yet is not identified by a SEQ ID number as required in 37 C.F.R. 1.821 through 1.825.

The examiner states that Applicants must submit a substitute paper copy of the Sequence Listing and an amendment directing its entry at the appropriate section of the specification.

The sequence referenced by the examiner at the above locations is LXXC. Applicants respectfully point out that 37 C.F.R. 1.821 indicates that the above Rules do not apply to this particular sequence: "Sequences with fewer than four specifically defined nucleotides or amino acids are specifically excluded from this section. 'Specifically defined' means those amino acids other than 'Xaa' and those nucleotide bases other than 'n' ...." (emphasis added) Applicants respectfully point out that the 3 letter code for the "X" in the LXXC sequence would be "Xaa," thus, these amino acids are not "specifically defined." The sequence recited has only 2 specifically defined amino acids. Therefore, does not need to be identified by a SEQ ID NO.

Applicants respectfully request that the requirement for a substitute sequence listing and amendment be withdrawn.

Objections

The abstract of the disclosure was objected to because of the number of words contained in the abstract exceeds the number of words permitted. Correction is required. See MPEP 608.01(b).

Current rules require the abstract to be 150 words or less. The abstract as amended contains less than 150 words.

The specification was objected to for the following reason(s):

(a) the first paragraph of the specification lacks the priority information as indicated above under the section "priority" in the Office Action. Amendment to the first paragraph of the specification is suggested.

A paragraph reciting the CROSS-REFERENCE TO RELATED APPLICATIONS has been added to include the priority information found in the PCT application.

(b) The use of trademarks in the instant specification has been noted. For example, see line 27 on page 42: "Sequenase"; line 17 on page 26 "Triton X-100" and "Tween..."; and lines 11 and 13 on page 24: "Tween-20." It is suggested that Applicants amend the whole specification and make necessary changes wherever trademark recitations appear.

The specification as amended includes indication of trademarks and service marks where it is believed they are necessary.

Rejection under 35 U.S.C. § 101

Claims 1, 15 and those dependent therefrom were rejected under 35 U.S.C. 101 because the claimed invention is alleged to be directed to non-statutory subject matter. The examiner states that claims 1 and 15, as written, do not sufficiently distinguish over peptides as they exist naturally because the claims do not particularly point out any non-naturally occurring differences between the claimed products and the naturally occurring products. In the absence of the hand of man, the naturally occurring products are considered non-statutory subject matter. See Diamond v. Chakrabarty, 447 U.S. 303, 206 USPQ 193 (1980). The claim(s) should be amended to indicated the hand of the inventor, e.g., by insertion of "isolated" or "purified" or "isolated and purified" as

is taught in the specification. See MPEP 2105.

Response

Claims 1 and 15, as amended, include the term "purified." This rejection should now be overcome.

Rejection under 35 U.S.C. § 112, 1st paragraph

Claim 2 was rejected under 35 U.S.C. 112, 1st paragraph as failing to provide an adequate written description of the invention and failing to provide an enabling disclosure, because the examiner alleges that the specification does not provide evidence that the claimed biological material is (1) known and readily available to the public; (2) reproducible from the written description, e.g., sequenced; or (3) deposited.

The examiner states that claim 2 is directed to a pneumococcal peptide that immunospecifically binds to a specific monoclonal antibody: 1B6E12H9; 3C4D5C7; 4E9G9D3; 4H5C10F3; 6F6F9C8; 8G12G11B10; and 1E7A3D7C2. The examiner alleges it is apparent that these monoclonal antibodies are required to practice the claimed invention. As required elements, the monoclonal antibodies must be known and readily available to the public, or be obtainable by a reproducible method set forth in the specification, or otherwise be available to the public. If the antibodies are not so obtainable or available, the enablement requirements of 35 U.S.C. 112, 1st paragraph, may be satisfied by a deposit of the hybridoma producing the monoclonal antibodies.

The examiner further states that from the specification on pages 12, 19, 27 and 40, it does not appear that the hybridoma producing the monoclonal antibodies recited as 1B6E12H9;

3C4D5C7; 4E9G9D3; 4H5C10F3; 6F6F9C8; 8G12G11B10; and 1E7A3D7C2 are deposited at a recognized depository. The monoclonal antibodies do not appear to the examiner to be readily available to the public and it is unclear if the cell line can be reproducibly isolated without undue experimentation. Since obtaining such a monoclonal antibody with the exact specificity for the peptide is alleged to be non-predictable, undue experimentation would be required to practice the invention. Without a publicly available deposit of the hybridoma cell lines, one of ordinary skill in the art could not be assured of the ability to practice the invention as claimed. Exact replication of: (1) a cell line; and (2) the cell line which produces the chemically and functionally distinct antibody is an unpredictable event. Deposit of the hybridoma producing the recited monoclonal antibodies would satisfy the requirements of 35 U.S.C. 112, 1st paragraph.

If a deposit has already been made under the provisions of the Budapest Treaty, filing of an affidavit or declaration by Applicants or assignees or a statement by an attorney of record who has authority and control over the conditions of deposit over his or her signature and registration number stating that the deposit has been accepted by an International Depository Authority under the provisions of the Budapest Treaty, that all restrictions upon public access to the deposit will be irrevocably removed upon the grant of a patent on this application and that the deposit will be replaced if viable samples cannot be dispensed by the depository is required. This requirement is necessary when deposits are made under the provisions of the Budapest Treaty as the Treaty leaves this specific matter to the discretion of each state. The specification should be amended to include complete deposit information for the hybridoma producing the recited antibodies, including the full address of the depository and the date of deposition. Additionally, Applicants are requested to amend the specification and the claim(s) with the proper information regarding the depository number and provide evidence to support the insertion for the depository number. The recitation of a

laboratory designation does not clearly define the recited monoclonal antibodies. Amending the claim to include the cell line deposit numbers following the laboratory designation is suggested.

Applicants' attention is directed to In re Lundack, 773 F.2d 1216, 227 USPQ 90 (CAFC 1985) and 37 C.F.R. 1.801-1.809 for further information regarding deposit practice.

Response

It is not entirely clear if the examiner intended to make a written description rejection in addition to an enablement rejection on the above grounds. The examiner states that the rejection includes "failing to provide an adequate written description of the invention" but the above reasoning appears to apply to enablement. For this reason, it is believed examiner has not met the initial burden for a written description rejection. Written description requires that the specification described the claimed invention in sufficient detail that one of skill in the art can reasonably conclude that the invention had possession of the claimed invention. MPEP 2163. The applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means that fully set forth the claimed invention. Possession may be shown in a variety of ways including description of an actual reduction to practice, or by showing that the invention was "ready for patenting" or by describing distinguishing identifying characteristics sufficient to show that the applicant was in possession. There is a strong presumption that an adequate written description of the claimed invention is present when the application is filed.

The claim must first be construed, then the entire specification reviewed to understand how applicant provides support for the various features of the claimed invention.

The enablement requirement is met if one of skill in the art is enabled to make and use that which is defined by the claims. MPEP 2164. The standard for determining whether the specification meets the requirement is "is the experimentation needed to practice the invention undue or unreasonable?" MPEP 2164.01; Mineral Separation v. Hyde, 242 U.S. 261, 270 (1916). The information in the application is coupled with information known in the art. The fact that experimentation may be complex does not necessarily make it undue, if the art typically engages in such experimentation. The In re Wands factors (which are not limiting) can be used to determine if there is sufficient evidence to support a determination that a disclosure does not satisfy the requirement.

Before any analysis of enablement can occur, the examiner must construe the claims. In order to make an enablement rejection, the examiner has the initial burden to establish a reasonable basis to question the enablement provided for the claimed invention. MPEP 2164.04.

Applicants first point out that claim 2 is not directed to the listed monoclonal antibodies themselves. Instead, the claim is directed to a peptide that immunospecifically binds to the listed monoclonal antibodies. This is true whether examining the claim for written description or enablement.

The hybridomas and their respective monoclonal antibodies are disclosed in U.S. Patent No. 5,854,416 as indicated in the specification (p. 12, lines 8-25). This patent has been incorporated into the present application specifically by incorporation by reference (see e.g., p. 12, lines 9-10, 21-22), as have all publications referenced throughout (p. 4, lines 11-14).

Antibodies can be prepared by many well-known methods (p. 11, lines 12-22; p. 12, lines 3-7). The monoclonal antibodies of the present invention are disclosed as indicated above as well as the following locations:

p. 19 line 31-p. 20, line 3

p. 23 line 29-p. 24, line 6

Example 1, p. 26, line 28-p. 28, line 9

Example 8, p. 40, lines 24-33

Example 12, p. 42, line 20-p. 43, line 9

For the above reasons, Applicants believe claim 2 is enabled and the rejection should be withdrawn. Furthermore, Exs. 9-12 demonstrate reduction to practice of more than one such peptide as claimed in claim 2. For this reason, Applicants also believe claim 2 meets the written description requirement.

Claims 6, 12, 15, 16, 18 and 20 were rejected under 35 U.S.C. 112, 1st paragraph as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection. The claims are viewed as not providing sufficient written description under 35 U.S.C. 112, 1st paragraph, for one to practice the invention.

The examiner states that one or more of the instant claims encompass a peptide having "at least 80% identical to a peptide whose sequence is SEQ ID NO: 6 or an immunogenic fragment thereof," or "a fragment of SEQ ID NO: 6." The specification intends therapeutic and diagnostic applications for the peptide, peptide fragment or the at least 80% identical peptide variant. The peptides claimed in claims 12, 16, 18, and 20 are required to confer "protective immunity against *S. pneumoniae*" infection. However, the specification, as originally filed, does not provide adequate written description that would allow one skilled in the art to obtain a peptide having at least 80%

sequence identity to the peptide of SEQ ID NO:6 and concurrently having the immunogenic and/or the protective ability against *S. pneumoniae*. There is no evidence within the instant specification describing how to obtain a peptide fragment, or a peptide variant having at least 80% sequence identity to SEQ ID NO:6, or a fragment thereof having the recited functional properties of immunogenicity and/or protective ability. With regard to the claimed peptide "fragment," neither the structural characteristics no the functional or biological characteristics of the claimed peptide fragment are disclosed. There is a lack of written description as to which specific fragment of the peptide of the amino acid sequence of SEQ ID NO:6 is encompassed in the claimed peptide fragment. The specification lacks written description as to whether retention of any fragment from any part of the 15 amino acid-long peptide of SEQ ID NO:6 (i.e., terminal or central parts) would yield a peptide fragment that would have the expected biologic, i.e., immunogenic and/or protective functions. Adequate written description is critical since the art reflects sensitivity of proteins to alterations of even a single amino acid in a sequence. For instance, Burgess et al. (J. Cell Biol. 111: 2129-2138 1990) teach that replacement of a single lysine residue at position 118 of acidic fibroblast growth factor by glutamic acid led to the substantial loss of heparin binding, receptor binding and biological activity of the protein. Similar teachings are provided by Lazar et al (Mol. Cellular Biol. 1988, 8: 1247-1252) who show that in transforming growth factor alpha, replacement of aspartic acid at position 47 with alanine or asparagines did not affect biological activity, while replacement with serine or glutamic acid sharply reduced the biological activity of the mitogen. Therefore, without a precise written description of the specific amino acid residues contained within the claimed peptide variant or a fragment thereof, one of ordinary skill in the art cannot be sure of the sequences embraced by the claims and would not be able to make and use those protein sequences or fragments as recited in the instant claims without undue experimentation. One of

ordinary skill in the art would not be able to make and use such peptide fragments or variants, for example, as a component of a therapeutic composition, without undue experimentation.

Response

To satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention. An applicant shows possession of the claimed invention by describing the claimed invention with all of its limitation using such descriptive means that fully set forth the claimed invention. Possession may be shown in a variety of ways including description of an actual reduction to practice or by showing that the invention was ready for patenting or by describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention. There is a strong presumption that an adequate written description of the claimed invention is present when the application is filed. Claim construction is an essential part of the examination process and the entire claim must be considered.

Though the language of the rejection states that it is a written description rejection, there is various language within the examiner's reasoning which relates to enablement instead (e.g., "allow one skilled in the art to obtain"; "how to obtain"; "would not be able to make and use ... without undue experimentation"). Applicants are somewhat unsure how to address the examiner's rejection since it relies at least partially on enablement standards. Therefore, the rejection is treated as strictly a written description rejection.

Claims 15, 16, and 18 contain the phrase "at least 80% identical to a peptide whose sequence is SEQ ID NO:6 or an immunogenic fragment thereof." All of the claims contain language regarding "an immunogenic fragment of SEQ ID NO:6."

The "therapeutic composition" in claims 12, 16, 18, and 20 include the limitation "wherein the therapeutic composition confers protective immunity against *S. pneumoniae* infection." The therapeutic composition comprises one or more of the peptides.

Contrary to the examiner's remarks, the specification teaches one of skill in the art how to obtain the listed peptides with at least 80% identity or immunogenic fragments thereof. The meaning of a peptide with at least 80% identity is readily apparent to one of skill in the art as well as an immunogenic fragment of the listed written-out sequences. The ordinary meaning to one of skill in the art and the definitions provided within the specification make these clear. (See also 112, 2nd remarks and, e.g., p. 19 to p. 22 including definition of "immunogenic fragment".) The structural and functional characteristics of the peptides which meet these criteria are clearly discerned from the given sequences, the knowledge of one of skill in the art, and the portions of the specification related to smaller portions of the full sequences including methods for making and identifying these smaller portions without explicitly writing out every possible fragment sequence or sequence of at least 80% identity within, for example, SEQ ID NO:6. The structural characteristics of the peptide fragments, i.e., the sequences, are found within the written out peptide sequences. One of skill in the art can readily envisage amino acid sequences within this larger sequence. Further, there are no critical elements which are missing from the claims. Applicants have provided sufficient structural and functional characteristics for one of skill in the art to see the Applicants had possession. Additionally, Applicants would draw an analogy to Example 14 of the Office's "Synopsis of Application of Written Description Guidelines" which demonstrates the written description requirement is met. Applicants respectfully request the rejection be withdrawn for the above reasons.

Claims 6, 12, 15, 16, 18 and 20 were rejected under 35 U.S.C. 112, 1st paragraph, because the specification, while being enabling for a composition comprising a 37-kDa protein of *S. pneumoniae* that confers protective immunity against a challenge with a wild-type *S. pneumoniae*, does not reasonably provide enablement for a peptide of SEQ ID NO:6, a fragment thereof, or a variant thereof having at least 80% sequence identity to SEQ ID NO:6 which is immunogenic and/or is able to confer protective immunity against challenge with a wild-type *S. pneumoniae*, as claimed. The specification does not enable a person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with the claims.

The examiner alleges that in the instant case, the claimed one or more peptides, the peptide fragment and the peptide variant having at least 80% sequence identity to the peptide of SEQ ID NO:6 are required to be immunogenic and/or are protective against *S. pneumoniae* for use in a therapeutic composition. The peptide, a fragment, or variant thereof as recited is intended for inducing a protective immune response to *S. pneumoniae* in a subject. Although a microbial polypeptide or protein is expected in the art to generally induce specific antibodies, the ability of peptides, undefined "fragments" or peptide variants having at least 80% sequence identity to the peptide of SEQ ID NO:6 to confer protective immunity against a microbial disease, pneumonia in the instant case, or to serve as a specific diagnostic reagent, is not predictable. The instant specification fails to teach how to produce a peptide "fragment" or a peptide having at least 80% sequence identity to the peptide of SEQ ID NO:6 such that it is capable of serving as a therapeutic composition and capable of conferring protective immunity to *S. pneumoniae* infection in a human or non-human subject. The specification provides no guidance as to which specific amino acids must be retained in a "fragment" or which may be varied in the peptide of SEQ ID NO:6 without

causing any detrimental effect to the claimed peptide that is meant to induce a protective immune response in a subject against *S. pneumoniae* infection. There is no guidance in the instant specification with regard to which amino acid variations, i.e., insertions, deletions, additions and substitutions, in the peptide would result in a peptide fragment or variant that would retain the functional integrity of biological/immunogenic competence of the native protein, without rendering it non-functional. There appears to be no evidence within the instant specification, as originally filed, showing the that peptide of SEQ ID NO:6, or fragment or variant thereof having at least 80% sequence identity to the peptide of SEQ ID NO:6, is capable of conferring protective immunity against *S. pneumoniae*. There appears to be not even a showing that the unmodified 15 amino acid-long peptide of SEQ ID NO:6, let alone its fragment or variant having at least 80% sequence identity, does indeed confer protective immunity against *S. pneumoniae*. A review of the specification suggests that the "Results" section on page 31 and Example 4 of the specification describe the protective ability of the 37-kDa protein of *S. pneumoniae*. Table 4 shows that the peptide of SEQ ID NO:6 is 1B6 mAb-specific. Example 14 shows that the peptide of SEQ ID NO:6 when conjugated to KLH and mixed with an adjuvant is immunogenic in mice. The protection experiments described in Examples 4 and 5 are limited to a showing that the whole 37-kDa protein of *S. pneumoniae* confers protection in mice against challenge with a wild-type *S. pneumoniae*. The specific monoclonal antibodies recited in the claims were generated using the 37-kDa protein. However, there is no showing that he peptide of SEQ ID NO:6, a fragment thereof, or a variant thereof having at least [sic] 20% dissimilarity to SEQ ID NO:6 is protective against *S. pneumoniae*. The immunogenicity of a fragment of the peptide of SEQ ID NO:6 or a variant of the peptide of SEQ ID NO:6 as recited is not established. This is important because the art reflects unpredictability as to which amino acids in a specific protein can be varied, i.e., replaced or added,

without adversely affecting the functional properties of that specific protein. While it is known in the art that variation in one or more amino acids is possible in a given protein, the exact position within its amino acid sequence where replacements or variations can be made, with a reasonable expectation of success of retaining the protein's functional integrity, is not certain. A random replacement affecting the epitopic amino acid positions that are critical, for example, to the three-dimensional conformational structure and specific binding property of the protein, would result in a polypeptide that may be non-functional (i.e., non-immunogenic) or not optimally immunogenic or protective as a vaccine candidate, because such positions tolerate no or little modifications. For instance, Houghton et al. (New Approaches to Immunization, Vaccines 86, Cold Spring Harbor Laboratory, p. 21-25, 1986) teach the criticality of individual amino acid residues and their positions in peptide antigen-antibody interactions. Houghton et al state (see page 24):

One could expect point mutations in the protein antigen to cause varying degrees of loss of protection, depending on the relative importance of the binding interaction of the altered residue. A protein having multiple antigenic sites, multiple point mutations, or accumulated point mutations at key residues could create a new antigen that is precipitously or progressively unrecognizable by any of the antibodies in the polyclonal pool.

Thus, the art reflects that variations in critical residues at specific positions in an amino acid sequence could result in a polypeptide which may induce an antibody that may not recognize or bind to the native polypeptide of a microorganism. In the instant case, this is important because one of the purposes of the invention is to produce a peptide of *S. pneumoniae* in its biologically active, immunogenic and/or protective form for inducing a protective immune response. The instant disclosure lacks guidance on the precise position(s), nature and extent of amino acid replacements or variations that can be made in the claimed peptide in order to produce a "fragment" or a variant

with 80% identity to SEQ ID NO:6, and with regard to whether it would serve as an effective immunogen capable of conferring protective immunity against *S. pneumoniae* infection in a human or non-human subject.

Therefore, undue experimentation would have to be required to reproducibly practice the full scope of the invention as claimed currently, due to the lack of adequate and specific guidance, the lack of evidentiary support in the specification enabling a functional "fragment" peptide or a variant peptide having at least 80% sequence identity to SEQ ID NO:6, the nature of the invention, the state of the prior art, the quantity of experimentation necessary and the art-demonstrated unpredictability in determining amino acid variations that are acceptable. Ex parte Foreman, 230 USPQ 546, 547 (BPAI 1986). One of ordinary skill in the art would no have been able to make a peptide fragment or a variant of the claimed peptide and use it, for example, for inducing anti-pneumococcal protective immune response in any subject, without undue experimentation, because there is no disclosure as to what positions and what specific amino acid residues are varied or truncated. The production and use of a fragment or variant of the peptide of SEQ ID NO:6 that is capable of inducing a protective immune response against pneumococcal infection(s) is well outside the realm of routine experimentation. The claims are viewed as not meeting the scope of enablement provisions of 35 U.S.C. 112, 1st paragraph.

Response

Legal requirements for enablement are discussed above.

The examiner states that "[t]he immunogenicity of a fragment of the peptide of SEQ ID NO:6 or a variant of the peptide of SEQ ID NO:6 as recited is not established," however, the examiner misses the fact that the peptides in the recited claims are by definition, and by explicit

recitation, immunogenic (see definition of "immunogenic fragment" and claims: "the peptide ... which is immunogenic"; "A therapeutic composition ...peptides that immunospecifically bind... and that are immunogenic against..."). The claims exclude those fragments or variants which are not immunogenic by their very terms, thus, only those operative peptides are covered.

Further, based on the guidance of the specification, e.g., "Epitopic Immunogenic Peptides" on pp. 16-23. For example, the peptide(s) can be identified and synthesized through a method such as that on pp. 17-18 and pp. 20-21. Also, claims 12, 16, 18, and 20 require the therapeutic composition to confer protective immunity; the peptides within the composition may or may not provide the only portion which confers the protective immunity. Page 19 discusses using similar procedures as described on pp. 17-18 in order to identify and produce an allelic immunogenic peptide. Methods for identifying immunogenic fragments are discussed, e.g., p. 22, lines 9-15. Methods for assessing the identified fragments for ability to elicit protective immunity is discussed, e.g., p. 22, lines 16-20. The guidance provided in the Examples such as Examples 4-7, 14 can be used to screen those identified peptides. Even if significant experimentation may be necessary, there is sufficient guidance within the specification to make the experimentation necessary to make and use the claimed peptides and compositions simply routine. Applicants respectfully request the rejection be withdrawn for the above reasons.

Rejection under 35 U.S.C. § 112, 2nd paragraph

Claims 1-6, 8-12, 15, 16, 18 and 20 were rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

Claims 6, 2 [sic], 15, and 20 were rejected as being vague and indefinite by the examiner in the recitation: "fragment," because it is allegedly unclear what is encompassed in this recitation. What constitutes a "fragment," and how much of the peptide's original structure has to be retained such that the resulting product can be considered as a "fragment" is not clear. The metes and bounds of the structure encompassed in the limitation "fragment" is indeterminate. Does a single amino acid, or a dipeptide qualify as a "fragment"?

Response

Applicants assume the reference to claim 2 is a typographical error since the term "fragment" does not appear in that claim. Applicants assume instead this is a reference to claim 12 and has been addressed under that assumption.

Applicants respectfully traverse the rejection because the term "immunogenic fragment" is defined in the specification on p. 22, lines 3-9. Specifically,

> "An immunogenic fragment is any peptide shorter than the peptide from which it is derived (the parent) whose sequence is identical to the sequence of a portion of the parent peptide and which retains immunogenicity. It is generally understood in the field of immunochemistry that such peptides must be at least about six residues long in order to be antigenic. Thus any fragment should be at least six residues in length and may have a maximum length one residue less than the parent peptide."

All of the recited claims either explicity state "an immunogenic fragment" or inherently refer to a "fragment" that is immunogenic due to the remainder of the claim language (i.e., peptide is "immunogenic" or "immunogenically binds..."). However, in order to expedite prosecution claims 6, 12, and 20 have been amended to "an immunogenic fragment" where the term "fragment" is

found. Claim 15 already explicity referred to "an immunogenic fragment." These amendments do not narrow nor broaden the claim scope and, therefore, have no Festo-type prosecution history estoppel effect.

Claims 1, 8, 12 and 20 were rejected as being vague and indefinite by the examiner in the use of abbreviated limitations in the claim language: "PsaA." It is suggested that the abbreviation be recited as a full terminology [sic] at the first occurrence, with its abbreviated recitation retained in parentheses.

Response

Applicants respectfully traverse the rejection because the abbreviation PsaA for pneumococcal surface adhesion A protein is clear from the specification (see, e.g., Field of Invention and Background). Thus, it is not necessary to write it out within the claim itself. However, in order to expedite prosecution claim 1 has been amended to spell out the PsaA and put the abbreviation in parentheses where used in its first instance in the claims. This amendment does not narrow nor broaden the claim scope and, therefore, has no Festo-type prosecution history estoppel effect.

Claim 15 was rejected as being vague by the examiner in the recitation "peptide comprising a sequence ... SEQ ID NO:...: without reciting that the sequence is an amino acid sequence. In order to distinctly claim the subject matter of the instant invention, it is suggested that Applicants replace the recitation with --peptide comprising an amino acid sequence ... SEQ ID NO: ... --.

Response

Applicants respectfully traverse the rejection because it is clear from the reference to "peptide" and by viewing the corresponding sequence that the sequence is, and would have to be, an amino acid sequence. Applicants believe that one of skill in the art would immediately see that the sequence is an amino acid sequence without addition of the words. However, in order to expedite prosecution claim 15 has been amended to include the words as suggested by the examiner. This amendment does not narrow nor broaden the claim scope and, therefore, has no Festo-type prosecution history estoppel effect.

Claims 6 and 15 were rejected as being vague by the examiner in the recitation "comprising residues whose sequence ... SEQ ID NO: ..." without reciting that the sequence is an amino acid sequence. In order to distinctly claim the subject matter of the instant invention, it is suggested that Applicants replace the recitation with --comprising residues whose amino acid sequence ... SEQ ID NO: ... --.

Response

Applicants are confused by the examiner's reference to claim 15 in this rejection as claim 15 does not contain the quoted language. Therefore, Applicants have not addressed claim 15 with regard to this specific rejection. Applicants respectfully traverse the rejection because it is clear from the reference to "peptide" and by viewing the corresponding sequence that the sequence is, and would have to be, an amino acid sequence. Applicants believe that one of skill in the art would immediately see that the sequence is an amino acid sequence without addition of the words. However, in order to expedite prosecution claim 6 has been amended to include the words as

suggested by the examiner. This amendment does not narrow nor broaden the claim scope and, therefore, has no Festo-type prosecution history estoppel effect.

Claims 12 and 20 were rejected as being vague by the examiner in the recitation "comprising residues whose sequences ... SEQ ID NO: ..." without reciting that the sequence is an amino acid sequence. In order to distinctly claim the subject matter of the instant invention, it is suggested that Applicants replace the recitation with --comprising residues whose amino acid sequences ... SEQ ID NO: ... --.

Response

Applicants respectfully traverse the rejection because it is clear from the reference to "peptide" and by viewing the corresponding sequence that the sequence is, and would have to be, an amino acid sequence. Applicants believe that one of skill in the art would immediately see that the sequence is an amino acid sequence without addition of the words. However, in order to expedite prosecution claims 12 and 20 have been amended to include the words as suggested by the examiner. This amendment does not narrow nor broaden the claim scope and, therefore, has no Festo-type prosecution history estoppel effect.

Claims 2-5, 9-11, 16 and 18, which depend directly or indirectly from claim 1, 6 or 15, are also rejected as being indefinite because of the vagueness or indefiniteness identified above in the base claim(s).

Response

This rejection should now be overcome as the rejections of claims 1, 6 and 15 have been overcome as discussed above.

Rejection(s) under Double Patenting

The non-statutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or impromper timewise extention of the "right to exclude"....

A timely filed terminal disclaimer ... may be used to overcome a[] ...rejection... provided the conflicting application or patent is shown to be commonly owned with this application.

Instant claims 1-6, 12, 15, 16, 18 and 20 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting over claims 1, 2, 8 and 12-14 of the application SN 09/613,092. Although the conflicting claims are not identical, they are not patentably distinct from each other because of their overlapping scope. The above-identified claims of the co-pending application, with regard to the peptide of SEQ ID NO: 10 claimed therein, fall within the scope of the peptide having 80% identity to SEQ ID NO:6 or an immunogenic fragment thereof, claimed in the instant claims.

Response

Since the scope of the claims of SN 09/613,092 may change (as well as the current claims) during the course of prosecution, Applicants respectfully request that a terminal disclaimer be postponed until the time of allowance in case such a disclaimer becomes no longer necessary.

Rejection under 35 U.S.C. § 102

Claims 1-5 and 8-11 were rejected under 35 U.S.C. 102(e) as being anticipated by Sampson et al. (U.S. 6,217,884).

The examiner alleges that Sampson et al disclosed a fragment (i.e., peptide) of a 37 kDa protein of *S. pneuomoniae* which is used as a vaccine component as well as a reagent for identifying host antibodies raised against *S. pneuomoniae* during infection. The specific monoclonal antibodies used are 1E7A3D7C2; 1B6E12H9; 3C4D5C7; 4E9G9C3 [sic]; 4H5C10F3; and 6F6F9C8 and 8G12G11B10 (see abstract; and column 7, lines 40-46; all of columns 11 and 12 including the paragraph bridging columns 11 and 12; and column 13, lines 1-46). The composition comprises a unique fragment (i.e., a peptide) of the 37-kDa pneumococcal surface adhesion protein (i.e., PsaA) for use in inoculating a host such that the polypeptide fragment generates an active immune response in the host which protects the host from infection (see column 13, seventh full paragraph). The composition comprises a pharmaceutically acceptable carrier and adjuvants (see column 14, lines 1-24). Synthetic peptides disclosed include shorter and larger peptides (see last paragraph in column 10) or partial polypeptides (see first full paragraph). The immunoreactive fragment of the 37-kDa pneumococcal surface adhesion protein is at least about 6 consecutive amino acids (i.e., inclusive of 10-15, 12-22 or 15 amino acid residues in length) having the ability to evoke an immune response (see lines 52-59 in column 11). The fragments are produced by selected modifications provided the immunogenicity of the peptide is not significantly impaired compared to the 37 kDa pneumococcal surface adhesion protein (see paragraph bridging columns 11).

Claims 1-5 and 8-11 are anticipated by Sampson et al.

Response

Applicants respectfully traverse this rejection. Applicants believe that the examiner has misread and misconstrued the recited claims:

1 (currently amended). A purified peptide that immunospecifically binds to a monoclonal antibody obtained in response to immunizing an animal with *Streptococcus pneumoniae* pneumococcal surface adhesion A protein (PsaA).

8 (original). A therapeutic composition comprising one or more peptides that immunospecifically bind to a monoclonal antibody obtained in response to immunizing an animal with *Streptococcus pneumoniae* PsaA, and an immunostimulatory carrier, wherein the therapeutic composition confers protective immunity against *S. pneumoniae* infection when administered to a subject.

The peptide and therapeutic compositions of claims 1-5 and 8-11 comprise a purified peptide that immunospecifically binds to a MAb obtained in response to immunizing an animal with PsaA. These particular claims are not drawn to the MAb itself (nor the PsaA itself nor fragments of PsaA), but instead a peptide that binds to the MAb.

Sampson et al. ('884) disclose an isolated nucleic acid (SEQ ID NO:1) encoding the 37 kDa *S. pneumoniae* surface adhesion A protein (SEQ ID NO:2), unique fragments of the nucleic acid encoding the protein (SEQ ID NO:1), and to the polypeptides encoded by the nucleic acids (SEQ ID NO:1). Also disclosed are antibodies to the polypeptides.

'884 at col. 7, lines 40-46 discloses the polypeptide of SEQ ID NO:2 and a polypeptide encoded by a nucleic acid comprising a unique fragment of at least 10 nucleotides of SEQ ID NO:1. Col. 11-12 disclose fragments of the 37 kDa PsaA. Col. 12-13 disclose an antibody (polyclonal or monoclonal) which binds with the polypeptide encoded by the nucleic acid SEQ ID NO:1 or

polypeptide encoded by a unique fragment of at least 10 nucleotides of SEQ ID NO:1. The antibody can be raised to the PsaA or a fragment of the PsaA Col. 13, lines 16-46 discloses a vaccine comprising an immunogenic polypeptide encoded by the nucleic acid SEQ ID NO:1 or polypeptide encoded by a unique fragment of at least 10 nucleotides of SEQ ID NO:1.

Applicants wish to point out the examiner's misreading of col. 10 in the '884 patent. The examiner states "[s]ynthetic peptides disclosed include shorter and larger peptides (see last paragraph in column 10) or partial polypeptides (see first full paragraph)." The full paragraphs in column 10 (lines 16-67) describe a method of producing a 37-kDa pneumococcal surface adhesion protein by linking two peptides or polypeptides together by protein chemistry techniques. These generic shorter and larger peptides and partial polypeptides may or may not be immunogenic. These shorter sequences are joined to form the 37-kDa protein itself.

This rejection should be withdrawn.

Claims 1, 6 and 15 were rejected under 35 U.S.C. 102(b) as being anticipated by Nuijens et al. (WO 91/17258) as evidenced by Harlow et al. (In Antibodies: A laboratory Manual. Cold Spring Harbor Laboratory, Chapter 5, p. 76, 1988).

It is noted that claims 1, 2 and 6 do not place a limit on the size or length of the peptide claimed.

Nuijens et al. disclosed a therapeutic or prophylactic composition comprising a peptide having the sequence, SYQHDL, which shows 100% (i.e., at least 80%) sequence identity with a fragment of the instantly claimed peptide of SEQ ID NO:6. See the attached sequence alignment; and Example II of Nuijens et al. The peptide is conjugated to a suitable carrier to enhance elicitation of an antibody response. Although Nuijens et al. are silent about the binding of the

peptide to a monoclonal antibody obtained in response to immunizing an animal with *S. pneuomoniae* PsaA as recited in claim 1, the prior art peptide sequence is viewed as the same as the Applicants' claimed peptide. The Office's position that Nuijens' peptide is the same as the Applicants' peptide is based upon the fact that every characteristic overlapping in Nuijens; and Applicants' disclosure are the same. In spite of the fact that Nuijens et al are silent about the binding of the peptide to a a monoclonal antibody obtained in response to immunizing an animal with *S. pneuomoniae* PsaA, since the prior art peptide is structurally the same as the instantly claimed peptide, the peptide is expected to bind immunospecifically to the Applicants' monoclonal antibody which was inaccessible to Nuijens et al. at that time. The property of binding to the specific monoclonal antibody recited by the Applicants is viewed as inherent to the peptide of Nuijens et al. due to the region of 100% sequence identity, the peptide of the prior art is expected to bind immunospecifically to a monoclonal antibody as recited, because the art recognizes that the smallest peptides which elicit antibodies that bind to the original full length protein are 6 amino acids in length. See the first sentence under "Size of the Peptide" on page 76 of Harlow et al. The Office's position that Nuijens' peptide is the same as the Applicants' peptide is based upon the fact that every characteristic overlapping in Nuijens' and Applicants' disclosure are the same. In spite of the fact that Nuijens et al. fail to teach all of the Applicants' disclosed functional characteristics, there is sufficient overlap to reasonably conclude that Nuijens' peptide is on and the same as Applicants' peptide. Since the prior art peptide is viewed as structurally the same as the instantly claimed peptide, it is expected to have the same properties as that of the instantly claimed peptide.

The teachings of Nuijens et al. anticipate the instant claims. Harlow et al. is not used as a secondary reference in combination with Nuijens et al., but rather is used to show that every element of the claimed subject matter is disclosed by Nuijens et al. with the unrecited limitation(s)

being inherent in view of what is known in the art as explained above. See In re Samour, 197 USPQ 1 (CCPA 1978).

Response

Nuijens et al disclose in Example II a peptide with the amino acid sequence

N-phe-ser-pro-val-**ser-tyr-gln-his-asp-leu**-ala-leu-C

This is a 12 amino acid peptide. SEQ ID NO:6 of the present invention is a 15 amino acid peptide:

Arg-**Ser-Tyr-Gln-His-Asp-Leu**-Arg-Ala-Tyr-Gly-Phe-Trp-Arg-Leu.

Claim 1 is drawn to

1 (currently amended). A purified peptide that immunospecifically binds to a monoclonal antibody obtained in response to immunizing an animal with *Streptococcus pneumoniae* pneumococcal surface adhesion A protein (PsaA).

Claim 6 is drawn to

6 (currently amended). The peptide described in claim 1 which is immunogenic against *S. pneumoniae* comprising residues whose amino acid sequence is chosen from the group consisting of ..., SEQ ID NO:6, ..., an immunogenic fragment of SEQ ID NO:6, ...

Claim 15 is drawn to

15 (currently amended). A purified peptide comprising an amino acid sequence which is at least 80% identical to a peptide whose sequence is chosen from the group consisting of ..., SEQ ID NO:6 or an immunogenic fragment thereof, ...

The sequence disclosed in Nuijens et al. does not anticipate the sequence SEQ ID NO:6. Though a portion of each sequence overlap, this is not enough to anticipate SEQ ID NO:6.

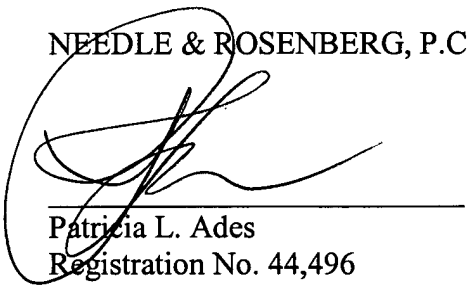
Further, the examiner has not shown that the sequence disclosed in Nuijens et al. anticipates any of the rejected claims. Note above that the fragment is an "immunogenic fragment" and a

peptide of claim 15 is one which is at least 80% identical to SEQ ID NO:6 or at least 80% identical to an immunogenic fragment of SEQ ID NO:6. The sequence alignment attached by the examiner shows a 40% query match for SEQ ID NO:6. It is not disclosed whether the 6 amino acid overlapping section of the Nuijens et al. peptide to the SEQ ID NO:6 peptide is immunogenic or immunogenic against *S. pneumoniae*. Nuijens et al. disclose that their sequence can produce antibody to Factor XII. The reference does not disclose whether the 6 amino acids within this sequence can produce antibody to Factor XII let alone whether this fragment of their sequence is immunogenic for *S. pneumoniae*. It has not been positively or negatively established that the 6 amino acid sequence **Ser-Tyr-Gln-His-Asp-Leu** is immunogenic. The examiner has not demonstrated whether the 6 amino acid sequence falls within the claims of the present invention.

A credit card payment form PTO-2038 authorizing payment in the amount of $110.00 for the fee for a one-month extension of time for a large entity and a request for the extension of time are enclosed. The amount is believed to be correct; however, the Commissioner is hereby authorized to charge any additional fee or credit any overpayment to Deposit Account No. 14-0629.

Respectfully submitted,

NEEDLE & ROSENBERG, P.C.



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CERTIFICATE OF MAILING UNDER 37 C.F.R. § 1.8

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Patricia L. Ades

Dec. 11, 2003
Date